



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

WASHINGTON, D.C. 20546

Marshall

JUN 21 1974

REPLY TO
ATTN OF: GP

TO: KSI/Scientific & Technical Information Division
Attn: Miss Winnie M. Morgan

FROM: GP/Office of Assistant General
Counsel for Patent Matters

SUBJECT: Announcement of NASA-Owned U.S. Patents in STAR

In accordance with the procedures agreed upon by Code GP and Code KSI, the attached NASA-owned U.S. Patent is being forwarded for abstracting and announcement in NASA STAR.

The following information is provided:

U.S. Patent No.

: 3,814,678
General Electric Co.
Philadelphia, PA

Government or
Corporate Employee

: _____

Supplementary Corporate
Source (if applicable)

: _____

NASA Patent Case No.

: MFS-71,395-1

NOTE - If this patent covers an invention made by a corporate employee of a NASA Contractor, the following is applicable:

YES ☒

NO ☐

Pursuant to Section 305(a) of the National Aeronautics and Space Act, the name of the Administrator of NASA appears on the first page of the patent; however, the name of the actual inventor (author) appears at the heading of column No. 1 of the Specification, following the words "...with respect to an invention of ..."

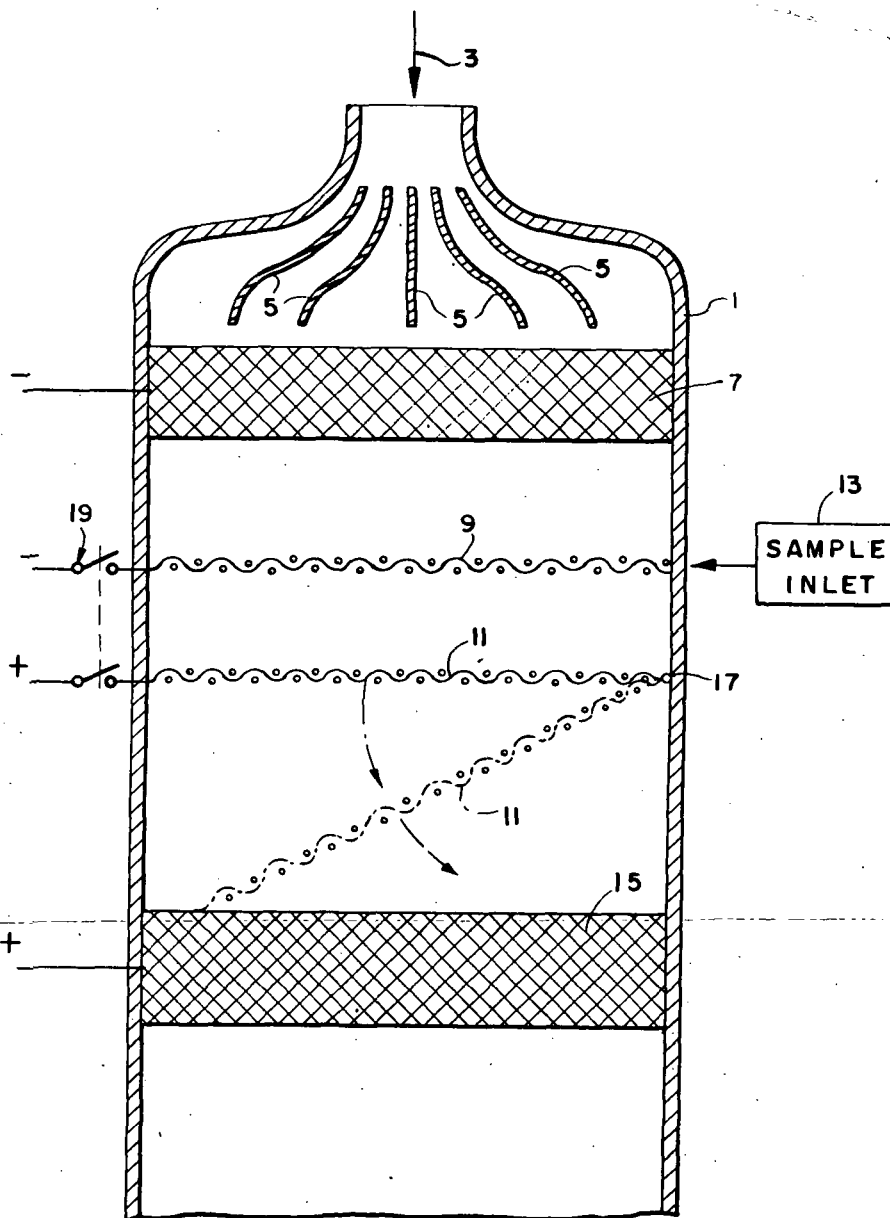
Bonnie L. Woerner

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Enclosure

June 4, 1974

JAMES C. FLETCHER
ADMINISTRATOR OF THE NATIONAL AERONAUTICS
AND SPACE ADMINISTRATION
ELECTROPHORETIC SAMPLE INSERTION
Filed June 6, 1972

3,814,678



3,814,678

(NASA-Case-MFS-21395-1) ELECTROPHORETIC
SAMPLE INSERTION Patent (NASA) 4 P

CSCL 14B

N74-26948

Unclas
00/14 40486

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3,814,678

ELECTROPHORETIC SAMPLE INSERTION
James C. Fletcher, Administrator of the National Aeronautics and Space Administration, with respect to an invention of Louis R. McCreight, Wayne, Pa.

Filed June 6, 1972, Ser. No. 260,093

Int. Cl. B01k 5/00

U.S. Cl. 204—180 R

6 Claims

ABSTRACT OF THE DISCLOSURE

Two conductive screens located in the flow path of an electrophoresis sample separation apparatus are charged electrically. The sample is introduced between the screens, and the charge is sufficient to disperse and hold the samples across the screens. When the charge is terminated, the samples are uniformly distributed in the flow path. Additionally, a first separation by charged properties has been accomplished.

ORIGIN OF THE INVENTION

The invention described herein was made in the performance of work under a NASA contract and is subject to the provisions of Section 305 of the National Aeronautics and Space Act of 1958, Public Law 85-568 (72 Stat. 435; 42 U.S.C. 2457).

BACKGROUND OF THE INVENTION

This invention relates to the electrical manipulation of materials and, more specifically, to the controlled distribution of materials having electrophoretic properties, specifically useful for sample insertion in an electrophoretic separation system.

Electrophoretic separation and fractionating systems are known in which the sample is inserted in a moving stream of buffer solution. In general, however, sophisticated techniques to introduce the sample are not employed and prior implantation of the sample on gels or the like is common. Unsatisfactory resolution and accuracy of prior, free-flowing-stream systems can be attributed to the fact that the sample is not precisely located in the system at proper areas in the design. Instead, it is not unusual to simply mix the sample with the buffer at a location prior to where the buffer with sample moves into the area of electrophoretic separation.

Where improved, free-flowing systems are developed for or made possible by a zero gravity environment, accurate and controlled sample placement is especially beneficial.

SUMMARY OF THE INVENTION

It is a primary object of this invention to provide an electrophoretic sample handling system and process which can be used for improved design in any system in which control of sample placement would be beneficial.

It is a somewhat more specific object of this invention to provide an electrophoretic sample placement system and process to distribute a sample evenly within a buffer flow path.

It is another, more specific object of this invention to provide an electrophoretic sample distribution system and process which effectuates a first separation of the sample.

It is a further, more general object of this invention to provide a system and process to insert a planar specimen in a continuous electrophoresis apparatus.

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In accordance with this invention two screens of conductive material are positioned across the area into which the sample is to be accurately placed. The screens are charged across a DC potential while the sample is introduced near the screens. The charge of the screens acts upon the components of the sample to physically move them through the screen into layers at different depths corresponding to the relative characteristics of the components. The charge of the screens is also made large enough to hold the sample against movement with buffer flowing through the apparatus or from other influences. The samples are released by reducing the charge to the screens. The charge provided to the screen farthest in the direction of flow of buffer is of the same polarity as the polarity of the farthest separation electrode. That screen may also be pivoted aside after the sample is released to minimize turbulence in the flow.

Other objects, features, advantages, and characteristics of the invention will be apparent from the following description of the preferred embodiment, as illustrated by the accompanying drawing.

BRIEF DESCRIPTION OF THE DRAWING

The drawing shows the major features of a continuous electrophoretic separator incorporating the preferred form of the sample insertion system.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Electrophoresis refers to the movement in an electric field of charged physical particles. The particles may be inherently charged in a given medium by surface effects or otherwise. Since movement of the particles is a function of charge, weight, and freedom of movement in the medium, particles of different characteristics may be separated by application of a DC field. The particles move relative to the DC field according to the combined effects of their characteristics and are separated as a result of the extent of movement which occurs.

The preferred form of the invention is employed in and adapted to a continuous electrophoretic separator or fractionator in which a buffer electrolyte solution is continuously passed through a conduit between separation electrodes and the sample is inserted at a location within the conduit. Flow of the buffer solution carrying the sample must be laminar and otherwise non-turbulent. Convection currents, sedimentation, and other disruptive phenomena are avoided in a low gravity or space environment, and the preferred device is employed in a zero gravity system. Such a low-gravity system has been originated by the inventor of this application and another, Richard N. Griffin, jointly, and is described and claimed in Application Ser. No. 258,171, titled Conducting Flow Electrophoresis in the Substantial Absence of Gravity. Major features particularly pertinent to this invention are shown in the drawing.

In the preferred separation system a buffered electrolyte carrier solution is continuously passed through a separation chamber, which may be straight or curved and which has a cross section configuration which minimizes turbulence, such as rectangular or circular. In the chamber the buffer is initially directed by baffles, porous plates, and other means into a uniform flow across the diameter of the chamber. The sample is subsequently inserted from one or more side ducts. The sample moves with the buffer

between the separation electrodes located at positions spaced along the flow path. The action of the charge on the separation electrodes moves the elements of the sample into disk-like layers which differ by their response characteristics, and the layers are extracted by valve control of a port in the side of the chamber. The system provide efficient retrieval of the buffer for reuse and excellent separations on a large enough scale to be considered for preparative use in the production of vaccines and other biological products.

With reference to the drawing, the preferred system is seen to comprise a central chamber or conduit 1, which may have any cross section tending to minimize turbulence, for example a rectangle 10 x 1. At the input port 3 a conventional buffered, liquid electrolyte is injected under pressure to serve as the carrier for the sample.

The buffer immediately encounters baffles or deflection members 5, which spread the buffer evenly in the chamber 1 and thereby foster laminar flow. The solution flows past the first separation electrode 7, which is an element effectively positioned across the chamber 1. Electrode 7 is connected to a DC potential selected in accordance with the charge of the elements of the samples to be separated to provide the desired separation; a negative potential is shown in the drawing as an example. (Electrode 7 is basically of conventional design and actually comprises an ion permeable membrane which forms a part of the side of the chamber 1 in a smooth connection and outline so as to encourage non-turbulent flow. An electrical member, connected to the DC source, and electrolyte, usually different from the buffer, are contained in a pocket outside of chamber 1. Passage of electrolyte through the semi-permeable material provides the necessary electrical communication.)

Past the electrode 7 in the flow path are the two, parallel conductive screens 9 and 11, positioned across the diameter of chamber 1 and spaced from each other. Screen 9, which is closest to electrode 7, is connected to a DC potential which is the same relative polarity as that of electrode 7 (negative in the example in the drawing). Screen 11, which is located farther down the flow path in chamber 1, is charged to the other polarity (positive in the example in the drawing).

Sample inlet 13, located in the area near screen 9 and 11, is adapted to insert samples periodically into chamber 1 from one or more ducts at the side. Inlet 13 is located to be close enough to screens 9 and 11 so that the charge on them dominates sample movement, and the sample is moved against the influences of both the moving buffer and the separation electrodes 7 and 15.

The second separation electrode 15 is spaced along the flow path a sufficient distance to permit elements of the sample to separate into layers under electrophoretic action on the flowing liquid. In the example in the drawing electrode 15 is connected to a positive potential. (Electrode 15 is substantially identical in structure to electrode 7. A semi-permeable membrane forms a smooth side to chamber 1 with the other elements of electrode 15 on the outside where they do not disturb fluid flow.)

Farther in chamber 1, past electrode 15, is situated a duct (not shown) through the side of the chamber 1 which is valved open and closed at selected times so that the layers of elements of the samples separated by the system may be extracted.

Screen 11 is attached to a hinge 17 or the like so that it may be rotated aside to remove it from the flow path and thereby facilitate further non-turbulent flow in the chamber 1. A switch 19 is shown as illustrative of electrical controls to activate and deactivate the field across screens 9 and 11.

In operation the buffer is fed under pressure continuously through inlet 3 and is recirculated and reused when it leaves the chamber 1. Baffles 5 function to disperse the buffer across the chamber 1. At periodic intervals sample is discharged from inlet 13 in the region of

screens 9 and 13, the times and amounts depending upon the various factors of a specific application, including the characteristics of the samples and the precision of separation desired.

When the sample is inserted, screens 9 and 11 are connected to DC potentials (switch 19 is closed or the equivalent), and the DC field across the screens 9 and 11 is strong enough to dominate sample movement over other factors, including the influences of buffer and the separation electrodes 7 and 15. The effectively charged elements of the sample disperse evenly across chamber 1. Also, a separation is made with those elements most affected by a positive field being moved to a layer closest to screen 11, those most affected by a negative field being moved to a layer closest to screen 9, and with other elements similarly positioned intermediate the two.

Subsequently, activation of the screens 9 and 11 is terminated by simply opening switch 19. To further facilitate non-turbulent flow, screen 11 may be slowly pivoted aside on hinge 17.

All elements of the sample then are free to move with the buffer and under the influence of the field across electrodes 7 and 15. Movement of the effectively charged elements of the sample is, essentially, the algebraic sum of the buffer movement and the movement in response to the field from separation electrodes 7 and 15.

Since the screens 9 and 11 provide a first separation of elements of the sample in the same order as that provided by electrodes 7 and 15, the electrophoretic separation is more pronounced than it would be without the screens 9 and 11. More importantly, the action of the screens 9 and 11 in evenly dispersing the sample across the chamber 1 greatly improves the precision of operation.

Variations of the invention described will be apparent, and variations may well be developed which employ more than ordinary skill in this art, but nevertheless employ the basic contribution and elements of the invention. Accordingly, patent protection should not be essentially limited by the preferred embodiments disclosed, but should be as provided by law, with particular reference to the accompanying claims.

What is claimed is:

1. The process of positioning electrophoretic samples comprising:

changing to a DC potential at least one conductive, screen-like member positioned in an area in which one said sample is to be positioned;

introducing said sample close enough to said member so that said potential dominates the movement of at least some elements of said sample;

subsequently reducing said potential; and

rotating said member to the side of the chamber after said reduction of potential.

2. The process as in claim 1 in which said area is in the chamber of a liquid-flow, electrophoretic separator system, at least one separation electrode is located in said chamber spaced from said area, and a separation by said electrode is effected after said reduction of potential.

3. The process as in claim 2 in which said electrophoretic separator system is a continuous flow system in which carrier flows through said screen-like member while said sample is introduced.

4. The process of positioning electrophoretic samples comprising:

charging to a DC potential at least one conductive member comprising two, generally parallel, screen-like members, positioned in an area in which one said sample is to be positioned, by applying a DC potential across said members;

introducing said sample close enough to said conductive member so that said potential dominates the movement of at least some elements of said sample;

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subsequently reducing said potential; and rotating said screen-like member, which is farthest along the flow path, to the side of the chamber after said reduction of potential.

5. The process as in claim 4 in which said area is in the chamber of a liquid-flow, electrophoretic separator system, and separation electrodes are located on each side of said area, and in which the electrode farthest along the flow path and the screen-like member nearest to it are charged in the same polarity, and a separation by said electrodes is effected after said reduction of potential.

6. The process as in claim 5 in which said electrophoretic separator system is a continuous flow system in which carrier flows through said screen-like members while said sample is introduced.

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U.S. Cl. X.R.

204—299, 300

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SECRET

